

Amendment under 37 C.F.R. § 1.116  
Application No. 10/527,694  
Attorney Docket No. 052203

**REMARKS**

(1) Claims 4, 6, 7, 11-13 are pending in this application, of which claims 4 and 11-13 have been amended. No new claims have been added.

Claim 4 has been amended to add “proteins” and polyamino acids.” These limitations were originally recited in claim 5. Claim 5 was already examined in the Office Action dated February 12, 2008. The limitations originally recited in claim 5 were inadvertently omitted in the amendment filed on May 12, 2008. The amendment of claim 4, as currently presented, does not necessitate further research so that the amendment of claim 4 should be entered. The amendment of claim 11 should be entered as well.

(2) Claims 12 and 13 were rejected under 35 U.S.C. §112, second paragraph. In response, claims 12 and 13 have been amended. Applicants believe that the amendment has overcome the rejection. Reconsideration of the rejection is respectfully requested.

(3) Claims 4, 6, 7 and 11 were rejected under 35 U.S.C. §103(a) as being unpatentable over Nagura et al. (JP 2000-212286) in view of Hermanson (chapter 3, entitled “Zero-Length Cross-Linkers”, PTO-892, Ref U).

(i) Hermanson teaches “Zero-Length Cross-Linkers.” *See* page 169. In case of the zero-length cross linkers taught by Hermanson, no intervening linker or spacer is attached as a result of the crosslinking reaction. In particular, Hermanson teaches that “the presence of these intervening linkers may be detrimental to the intended use.” *See* page 169, the 1st paragraph. In other words, Hermanson teaches causing direct crosslinkage between the carboxyl groups (e.g., glutamic acid and asparagine acid) and amino acids (derived from lysine) included in collagen and gelatine. As shown in Figures 107 and 108, Hermanson teaches “Zero-Length Cross-Linkers” which causes a crosslinking reaction with no intervening linkers. Hermanson teaches adding sulfo-NHS (N-hydroxysulfosuccinimide) to the protein. *See* Protocol 4 at page 175.

The teaching by Hermanson does not meet the limitations of “biological low-molecular-weight compound,” and “modifying at least one carboxyl group of malic acid, oxalacetic acid, citric acid, or *cis*-aconitic acid,” as recited in claims 4 and 11. For example, claim 4 recites “a crosslinked high-molecular-weight product obtained by crosslinking a high-molecular-weight compound with a biological low-molecular-weight compound.” “The biological low-molecular-weight compound is obtained by modifying at least one carboxyl group of malic acid, oxalacetic acid, citric acid, or *cis*-aconitic acid with N-hydroxysuccinimide or N-hydroxysulfosuccinimide.” Because of using a biological low-molecular-weight compound from at least one carboxyl group of malic acid, oxalacetic acid, citric acid, or *cis*-aconitic acid, the claimed “biological low-molecular-weight compound” is low molecular weight, as claimed. The

claimed invention is not directed to a zero-length cross linkers as taught by Hermanson. Rather, since a linker remains after crosslinking reaction, such an invention is taught away by Hermanson. Hermanson teaches that “the presence of these intervening linkers may be detrimental to the intended use,” *see* page 169, the 1st paragraph; and teach a zero-length cross linkers.

Moreover, the crosslinked high-molecular-weight product obtained by the claimed crosslinking process is distinct from the crosslinked product of Hermanson. The crosslinked high-molecular-weight product of claim 4 includes a low molecular weight compound as a result of the crosslinking reaction, while the crosslinked product of Hermanson does not include any linker since Hermanson teaches a zero-length cross linkers.

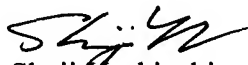
(4) In view of above, Applicants submit that that the claims, as herein amended, are in condition for allowance. The claimed invention is not obvious over the teaching by Hermanson. Thus, the invention of claims 4 and 11 cannot be obtained by combining Nagura et al. with Hermanson.

Applicants request such action at an early date. If the Examiner believes that this application is not now in condition for allowance, the Examiner is requested to contact Applicants' undersigned representative at the telephone number indicated below to arrange for an

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interview to expedite the disposition of this case. If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,  
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